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PATENT
015280-325200US
E-157-97/2

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Rybak *et al.*

Application No.: Unassigned

Filed: Herewith

For: IMMUNOTOXINS DIRECTED
AGAINST MALIGNANT CELLS

Examiner:

Art Unit:

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to examination of the above-referenced application, please enter the following amendments and remarks.

Please amend the application as follows.

IN THE CLAIMS:

Please cancel claims 13 and 27-34. Please replace claims 1 and 26 with the following clean version of the amended claim. A marked up copy showing the amendment to claims 1 and 26 is provided as Appendix A. For convenience, all of the pending claims are provided hereinbelow.

1. (amended) A selective cytotoxic reagent comprising an onc protein having measurable ribonucleolytic activity covalently linked to an antibody directed against a surface marker specific to a B cell, wherein the cytotoxic reagent is at least 100 times more cytotoxic to

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target cells bearing a B cell marker than a comparison reagent comprised of the same antibody joined to the human non-toxic RNase eosinophil-derived neurotoxin (EDN).

2. The reagent of claim 1, wherein the onc protein has the amino acid sequence of SEQ ID NO:1.
3. The reagent of claim 1, wherein the onc protein is produced by recombinant means.
4. The reagent of claim 3, wherein the onc protein has the amino acid sequence of SEQ ID NO:3
5. The reagent of claim 3, wherein the onc protein is encoded by the nucleic acid molecule identified as SEQ ID NO:2.
6. The reagent of claim 1, wherein the antibody is a monoclonal antibody.
7. The reagent of claim 6, wherein the monoclonal antibody is humanized.
8. The reagent of claim 7, wherein the monoclonal antibody is a single chain antibody.
9. The reagent of claim 1, wherein the antibody is specific for B cell lymphomas.
10. The reagent of claim 9, wherein the antibody is selected from the group consisting of RFB4 and LL2.
11. The reagent of claim 1, wherein the surface marker is CD22.
12. The reagent of claim 1, wherein the surface marker is CD74.

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13. (cancelled) The reagent of claim 12, wherein the antibody is LL1.
14. The reagent of claim 1, wherein the onc protein is conjugated to the antibody through recombinant fusion.
15. A nucleic acid sequence encoding the reagent of claim 1.
16. A pharmaceutical composition comprising a selective cytotoxic reagent comprising an onc protein having measurable ribonucleolytic activity joined to an antibody directed against a cell surface marker specific to a B cell together with a pharmaceutically acceptable carrier.
17. The pharmaceutical composition of claim 16, wherein the onc protein has the amino acid sequence of SEQ ID NO:1.
18. The pharmaceutical composition of claim 16, wherein the onc protein is produced by recombinant means.
19. The pharmaceutical composition of claim 18, wherein the onc protein has the amino acid sequence of SEQ ID NO:3.
20. The pharmaceutical composition of claim 18, wherein the onc protein is encoded by the nucleic acid molecule identified as SEQ ID NO:2.
21. The pharmaceutical composition of claim 16, wherein the onc protein is conjugated to the antibody through recombinant means.
22. The pharmaceutical composition of claim 16, wherein the antibody is a monoclonal antibody.
23. The pharmaceutical composition of claim 22, wherein the monoclonal antibody is humanized.

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24. The pharmaceutical composition of claim 23, wherein the monoclonal antibody is a single chain antibody.

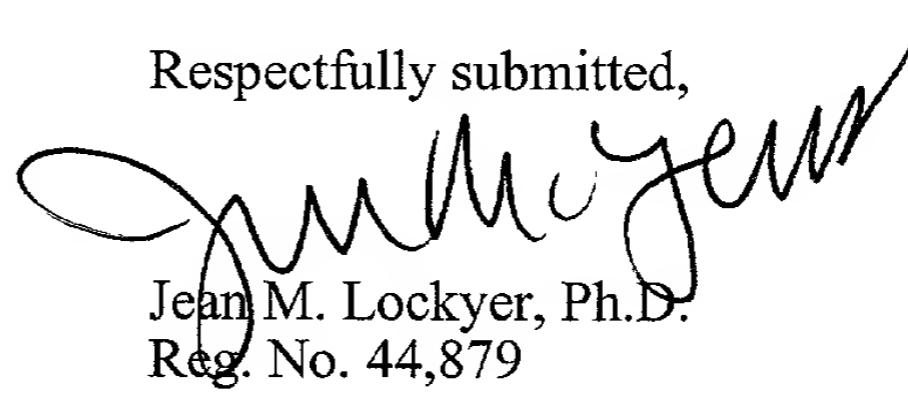
25. The pharmaceutical composition of claim 16, wherein the antibody is directed against a surface marker present on B cell lymphomas.

26. (amended) The pharmaceutical composition of claim 25, wherein the antibody is selected from the group consisting of RFB4 and LL2.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (amended) A selective cytotoxic reagent comprising an onc protein having measurable ribonucleolytic activity [joined] covalently linked to an antibody directed against a surface marker specific to a B cell, wherein the cytotoxic reagent is at least 100 times more cytotoxic to target cells bearing a B cell marker than a comparison reagent comprised of the same antibody joined to the human non-toxic RNase eosinophil-derived neurotoxin (EDN).

26. The pharmaceutical composition of claim 25, wherein the antibody is selected from the group consisting of RFB4[, LL1] and LL2